011 COMPLIANCE ACTIVITIES

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FACTORY INSPECTIONS

FDA determines compliance with the medical device regulations primarily by factory inspections. During the inspection, the FDA investigator will review your facilities, design controls, manufacturing operations, environment, and records to determine your level of compliance. The major emphasis will be on compliance with the Quality System (QS) regulation. Thus, it is important that manufacturers develop, maintain and use a quality system as outlined in this manual.

Inspection Plan

Manufacturers should be familiar with the QS regulation. Prior to an inspection, you may want to conduct an audit of your manufacturing operations and processes, or have an audit performed by a qualified auditor who is not associated with the firm. Any deficiencies identified should be corrected and implemented prior to the FDA inspection. Manufacturers should not depend on an FDA inspection to do this QS assessment for them. FDA performs pre-announced inspections for firms with no adverse compliance history. After the firm has become familiar with

the QS regulation, they should develop an internal plan for dealing with inspections (FDA, ISO, etc.). The plan should detail the manufacturer's policy regarding inspections, and designate the specific individual(s) who will accompany and/or assist the investigator. Receptionists should be informed when an investigator is scheduled to visit the facility and instructed as to who is to be contacted once the investigator arrives.

Sample of a letter to pre-announce an FDA international inspection. Footnotes added to sample letter.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

U.S. Food and Drug Administration
Division of Emergency
and Investigational Operations
Medical Device and Foods Section
5600 Fishers Lane RM: 13-71/13-85
Rockville, MD 20857 U.S.A.

Telephone: 301-827-5653 or 5632
Telefax: 301-443-6919

Number of Pages Sent 2

DATE:

TO:

FAX:

ATTN:

Dear _____

I am writing to pre-announce an inspection of the above referenced firm by an inspector of the U.S. Food and Drug Administration. This will be a _____ * inspection covering the FDA's Current Quality System/Good Manufacturing Practice Regulations for Medical Devices (21 CFR Part 820) and is part of our effort to inspect foreign manufacturers that export their products to the United States.

There is no cost to your firm for this inspection. However we do ask that an English speaking member of your staff or interpreter be made available during the inspection.

We are scheduling an inspector to be in your country during the month of _____. The proposed dates to conduct this inspection are as follows:

Footnotes:

Inspections of medical device firms will cover all applicable sections of 21 CFR Part 820 as they pertain to your firm.

* Usually a GMP inspection for glove manufacturers.
Design Controls apply to surgeon's gloves per 21 CFR §820.30(a)(2)(ii).

If this site does not have the research and development or specification developer (i.e., you believe design controls are not applicable), please provide the following information:

R & D or Specification Developer:

Firm Name:
Address:
City, Country:
Contact Person:
Phone Number:
Fax Number:

Please confirm receipt of this message, and that these dates are suitable by return fax **as soon as possible**.

Upon confirmation I may also ask for your assistance in arranging for hotel accommodations and transportation to and from your plant on the days of the inspection.

Thank you in advance for your attention to my request and I look forward to hearing from you shortly. If I can be of assistance, please do not hesitate to contact me at 301-827-5632.

Sincerely,

Liliane Brown
Associate Director

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Conduct During the Inspection

Upon arrival at your facility, the investigator will present his/her credentials and issue an FDA 482, Notice of Inspection, to the most responsible person at the facility. FDA does not issue Notices of Inspection for foreign inspections. If a foreign manufacturer refuses an inspection without a valid reason, their devices are adulterated per §820.1(d) and FDA may detain their devices at the U.S. port of entry. The manufacturer should examine the FDA investigator's credentials. Then, the receptionist or initial contact persons should inform all key employees that an FDA investigator is present.

If the investigator is not familiar with the manufacturer, the contact person should describe the product line and operations, and review their policies and programs with the investigator. During the inspection, the investigator may continuously record his/her observations. The FDA investigator will provide a written list of any significant observations (deviations from the QS Regulation) at the close of the inspection. These observations will be placed on form FDA-483, "Inspec-

tional Observations." If your representative disagrees with any observation made by the FDA investigator, be sure to discuss the reason for the observation with the investigator. You may find that there was a misunderstanding that can easily be corrected. These observations will be discussed with the manufacturer's management.

During the inspection the FDA investigator may hold a discussion with firm representatives at the end of each day. This provides time for the investigator to tell the firm about any problems or concerns they have with the areas covered during the inspection to date to clarify any misunderstandings that may have occurred.

A company individual should accompany the investigator any time they are in the production areas, reviewing documents, or talking to firm employees about the inspection. Understanding what the investigator is inspecting is an important part of handling an FDA inspection. Comments and suggestions made by the investigator, unanswered questions, and promises should all be recorded. The firm should be taking their own notes on the general areas of the plant visited by the investigator, whom they spoke to, the documents reviewed, and copies. This information can help management to prepare their comments in response to any deviations listed on the form FDA-483 at the conclusion of inspection.

If any records copied by an investigator contain trade secret or otherwise confidential information, these records should be identified, i.e., by a confidential stamp. Do **NOT** automatically mark every page of a document as confidential. This information is used by FDA in determining if the record may be released under the Freedom of Information Act.

Occasionally during a domestic inspection, the investigator may collect exhibits to document conditions in the factory, or collect samples to verify product quality, or to investigate user complaints. Whenever an investigator collects samples, duplicate samples should be collected and stored by your company. Before leaving your premises with a sample, the investigator will issue a form FDA-484, "Receipt for Samples." Where indicated, the investigator will obtain copies of shipping records to document interstate movement of shipments from which these samples were taken. The investigator will then prepare the appropriate FDA affidavit form (forms FDA 463a, 463, 1664a, or 1664b) which will reference these shipping records. A responsible employee of the firm will be asked to verify, by signature, that the documents referenced in the affidavit pertain to the shipment(s) in question.

Each employee should understand the investigator's questions before answering. If needed, ask for an explanation. Refer each question to the most suitable employee. Questions should be answered by employees who are knowledgeable in the area related to the question. If there are questions for which you don't have an immediate answer, make a list of these unanswered questions, get the answers, and give them to the investigator.

During the inspection, the firm can implement corrective action on any QS regulation deficiencies noted by the investigator with which they agree. The investigator should be made aware of any corrections after they are implemented because these corrections will show intent to comply with the FDA regulations.

Close-out Meeting

At the end of a factory inspection, the FDA investigator conducts a close-out meeting. During this meeting, the investigator will discuss the observations recorded on form FDA-483 with the manufacturer's management. Representatives of the firm will be given a copy of the completed form FDA-483, which should be checked for accuracy and completeness against their notes. If no FDA-483 is issued, the investigator will discuss his/her findings in general. Management with executive responsibility should be present to answer questions about any corrective actions to be taken and schedules for these actions. The firm has an opportunity to have the form FDA-483 annotated by the investigator with one of four select annotations based on the firm's responses: corrected and verified; reported corrected, not verified; promised to correct; or no comment. If a firm does not wish to have the form FDA 483 or any particular observation annotated, they should let the investigator know.

The investigator should be reminded of any corrections that have been made. Discuss your plans to make corrections, and provide a tentative schedule for these future actions. Answers given at this meeting will be recorded by the investigator. During the close-out meeting, make sure that all deviations are adequately discussed. If there is disagreement, present all of the manufacturer’s information and any regulations and official FDA interpretations that support your viewpoint.

After the Inspection

It is imperative that the manufacturer respond to any recommendations or observations made by the FDA investigator or other official. If you disagree with an observation, include your reason and supporting documentation, regulations, and/or official FDA interpretations. A written response to the form FDA-483, along with documentation to show how the manufacturer has corrected or intends to remove or correct the objectionable conditions or practices, can help assure the FDA that the manufacturer has corrected or intends to correct listed violations. A clear, quick response will demonstrate the manufacturer’s intent to comply with the medical device regulations. You should prepare a response even if you do not receive anything from FDA in writing. To repeat, a plan of corrective action is very important. Domestic manufacturers may also request a meeting with FDA district management to discuss violations and your proposed courses of action. This approach allows you to present your case to the FDA.

Foreign manufacturers should provide their response, including their rationale for any unresolved items to:

FDA/CDRH (HFZ-306)
2094 Gaither Road
Rockville, MD 20850 U.S.A.

A post-inspectional letter will be sent to the firm by FDA indicating the firm’s state of compliance such as no action indicated (NAI) or voluntary action indicated (VAI). FDA will mail a completed Establishment Inspection Report (EIR) to management of the firm after FDA determines that the inspection is closed.

FDA REGULATORY SANCTIONS

Management Letter

If management with executive responsibility is not present during the issuance of the form FDA-483 at the end of the inspection, FDA may send a "Management Letter" to company management with executive responsibility to assure that they have a copy of the issued form FDA-483. The Management Letter is only a brief transmittal letter, and is not to be confused with the "Warning Letter" described below.

Warning Letter

A Warning Letter is a specifically-worded enforcement letter written by top management of an FDA field or headquarters unit to management with executive responsibility for a firm. The letter is sent by FDA to a manufacturer primarily to draw the manufacturer's attention to violations and thereby, obtain prompt correction. A Warning Letter is intended to obtain correction of deficiencies noted:

- during an inspection,
- from an investigation of a product complaint, or
- from information received from other sources.

A Warning Letter may be issued by FDA instead of immediately seizing the product, obtaining an injunction, or detaining imports. The Warning Letter contains a formal warning to the manufacturer that specific sections of the law have been violated and unless corrective action is taken, the FDA is prepared to impose legal and/or administrative sanctions. Domestic sanctions include seizure, prosecution, injunction, and civil penalties. Unless otherwise indicated, within 15 working days after receiving a Warning Letter, a formal response must be made by the manufacturer to FDA. If you receive a Warning Letter, you should respond by stating the specific steps your organization has taken to correct noted violations, including an explanation of each action to prevent recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and when the correction will be completed.

A Warning Letter is also considered to be a prior warning and notification to responsible officials of the company of possible civil or criminal action to be taken by FDA.

Responsible individuals should not assume they will always receive a Warning Letter before FDA initiates administrative action or recommends an injunction, seizure, civil penalty and/or criminal proceeding. Before initiating formal regulatory action, FDA is under no legal obligation to warn manufacturers or individuals that they or their products are in violation of the law. For example, the FDA ordinarily will not issue a Warning Letter but will take other action such as seizure and injunction when:

- the violation reflects a recent history of repeated or continuous conduct of a similar or substantially similar nature during which time the manufacturer and/or individual(s) have been notified of a similar or substantially similar violation,

- the violation is intentional or flagrant, or
- the violation represents a reasonable possibility of injury or death.

An FDA Warning Letter to a manufacturer does not preclude initiation of other concurrent action, such as seizure or administrative detention, as part of an overall enforcement strategy.

Seizure

A seizure is a civil court action against a specific quantity of goods whereby FDA seeks to remove these goods from commercial channels. After seizure, no one may move or tamper with the goods except by permission of the court. The owner of the seized merchandise is usually given approximately 30 days by the court to decide on a course of action. If no action is taken and the owner does not file a claim to the goods, the court generally will recommend disposal of the goods. If the owner decides to contest the Government's charges and files a claim to the goods, the case will be scheduled for trial. A third option allows the owner of the goods to request permission of the court to bring the goods into compliance with the law. In this situation, the owner/claimant of the goods is required to provide a bond (money deposit) to assure that the orders of the court will be performed, and the owner/claimant must pay for FDA supervision of any activities by the manufacturer to bring the goods into compliance.

Administrative Detention

An administrative detention prohibits the distribution or use of adulterated or misbranded devices encountered during inspections. The detention usually lasts up to 30 days, possibly longer, until FDA has considered what action it should take concerning the devices, or has initiated legal action if appropriate. During the detention, detained devices may **not** be used, moved, altered, or tampered with in any manner by any person.

Restraining Orders and Injunctions

A "Temporary Restraining Order" (TRO) may be sought by FDA before an injunction and is designed to stop the alleged violative practice until the court can hear evidence that may lead to an injunction. A TRO imposes restraint upon a defendant for not more than 10 days, although this period may be extended by the courts.

An injunction is a court order that restrains a person or manufacturer from violating the law, e.g., to prevent interstate distribution of violative products, and to correct conditions in the establishment in which the violation occurred.

FDA STATUTORY AND REGULATORY REQUIREMENTS FOR MEDICAL GLOVES

When patient examination gloves and surgeon's gloves were initially classified by FDA, patient examination gloves were exempted from 510(k) premarket notification and medical device good manufacturing practices.

On January 13, 1989, the FDA published regulations in the *Federal Register* which removed the exemptions from 510(k) and QS regulatory requirements. On December 12, 1990, regulations were published which specified defect levels for adulteration of patient examination and surgeon's

gloves (21 CFR 800.20). Prior to the passage of this regulation, FDA initiated inspections of glove manufacturers to assure adherence to medical device QS requirements and initiated a comprehensive testing program to assure conformance to acceptable defect levels. FDA sampling methodology and defect action levels are detailed in the FDA Compliance Policy Guides, Chapter 3, Devices, Subchapter 335, General Hospital, Section 335.700, *Surgeon's Gloves and Patient Examination Gloves; Defects - Criteria for Direct Reference Seizure*. This guide is included at the end of this chapter.

The FDA test method for gloves is detailed in 21 CFR §800.20, which is reprinted at the end of this chapter. This rule states that FDA's analysis of gloves for leaks is conducted by a water leak method, using 1000 milliliters (ml) of water. Each medical glove is analyzed independently. When packaged as pairs, each glove is considered separately, and both gloves are analyzed. A defect in one of the gloves is counted as one defect; a defect in both gloves is counted as two defects. Defects are defined as leaks, tears, mold, embedded foreign objects, etc. A leak is defined as the appearance of water on the outside of the glove. This emergence of water from the glove constitutes a watertight barrier failure. Leaks or defects within 1½ inches of the cuff are disregarded. A glove with multiple quality problems such as a hole, mold, embedded foreign objects, etc., is counted as one defective glove.

COMPLIANCE ACTIVITIES FOR IMPORTED GLOVES

The FDA periodically performs inspections of foreign manufacturers, typically with the permission and cooperation of the manufacturer and foreign government. FDA cannot impose the same regulatory sanctions upon foreign manufacturers that it can upon U.S. manufacturers, e.g., injunction or prosecution. If a foreign manufacturer refuses to permit or allow the completion of an FDA inspection, its devices will be considered adulterated under section 50l(h) of the FD&C Act and will be detained at the point of entry [see 21 CFR 820.1(d)].

Section 801 of the FD&C Act details FDA's authority over imported devices. FDA is authorized to examine samples of incoming medical devices, and refuse entry to products that appear to be adulterated or misbranded. This includes apparent non-compliance with medical device QS requirements as well as sample analyses confirming device defects in excess of specified defect levels. At import, various information will be needed to identify the shipment and to verify its status. To reduce import delays, invoices should reflect the following under "Description of Entry:"

- Foreign manufacturer's listing number (form FDA 2892),
- U.S. importer's registration number (form FDA 2891),
- Premarket notification [510(k)] number, and
- Notes covering any change of the manufacturer's name or transfer of a 510(k).

Please note that the FDA Modernization Act of 1997 also requires foreign manufacturers exporting medical devices to the U.S. to be registered (form FDA 2891).

You should also confirm that on invoices, shipping records, etc.:

- The name on the device matches the name on the listing form FDA 2892;
- The name of the manufacturer of the device matches the name on the listing form;
- The 510(k) number on records, or if requested by FDA, is correct for the device at the port of entry;
- Information on outer shipping containers matches the information on immediate packaging, such as dispenser boxes; and
- Contain information about any change of the manufacturer's name or purchase of a factory with a 510(k).

When a shipment of a foreign manufacturer's gloves is presented for import, the FDA district office may elect to sample the shipment for testing. When this occurs, the importer of the gloves will receive a Notice of FDA Action. Upon receipt, the importer should contact the detaining district if he wishes to move the shipment to his own premises or to a warehouse of his choice. The importer **should not** distribute the gloves until they are tested and released. **Remember**, these gloves are not legally entered into the U. S. until a notice of release is issued by the FDA. If the gloves fail FDA testing, the importer will be asked to account for all gloves in the shipment. If some of the gloves have been distributed and cannot be accounted for, the importer may incur a penalty based upon his/her failure to redeliver the goods to the U.S. Customs Service.

If any lots of medical gloves are found to be adulterated or misbranded, the manufacturer or importer of record must bring them into compliance. He/she should advise the FDA district that initiated the detention of the firm's plans for bringing the product into compliance. If the product cannot be brought into compliance, it cannot be marketed in the U.S. as medical gloves.

Non-conforming medical gloves may be brought into conformance by:

- Re-exporting to the country of manufacture or to a country where the gloves would meet local requirements;
- Destroying, usually via landfill;
- Reconditioning to correct the non-conformance, i.e., remove defective gloves, labeling deficiencies corrected; or
- Reconditioning by relabeling, and subsequently distributing the gloves for non-medical use, or non-FDA regulated use.

If the manufacturer/importer chooses to recondition the product, they must request and obtain permission from the responsible FDA District Office.

One method of reconditioning out-of-compliance medical gloves may be to **label and market** them for use in food handling or preparation. Another method may be to **label and market** such gloves for non-FDA regulated use, such as household gloves, painter's gloves, etc. If relabeling the product for a non-FDA regulated use, be careful to remove all inferences that the product may be suitable for an FDA regulated use. This may even include modifying reference to an establishment name. For example, Topgrade Medical Glove Supply Corporation or International Hospital Glove Supply Company would **not** be suitable establishment names on the labeling of gloves being reconditioned for non-FDA regulated use.

DETENTION

Administrative Detention

Detention is the administrative action taken by FDA in accordance with its regulations at 21 CFR 800.55 against imported medical devices that are not in compliance with the laws which FDA administers. Imported medical devices may be detained whenever physical examination or testing of a medical device, or examination of medical device labeling and labeling claims by FDA reveals the medical device to be in violation of FDA laws. The importer of record may file an appeal requesting an informal hearing at which a presiding FDA officer shall affirm or revoke the detention. Detained devices are either released if brought into compliance, or refused entry if not brought into compliance.

For information about importing and exporting medical devices, please see our International web site at: http://www.fda.gov/cdrh/international/

Detention Without Physical Examination

Detention Without Physical Examination (DWPE) is the administrative act by FDA of detaining the entry of a specified article, usually from a specific supplier, and occasionally from all suppliers from a specific country, **without physical examination or testing.** DWPE differs from general administrative detention in that it is imposed based on the previous violative history of an imported medical device being offered for entry into the U.S. and does not occur as a result of a violative analysis or elimination of the present entry found by FDA. DWPE is an effective action used against severe or chronic violations or violators. It is also an effective control for those importers that expect the FDA to serve as a quality control laboratory for them. DWPE essentially places the responsibility for determining quality and compliance with the law upon the U.S. importer or broker, and indirectly upon the foreign supplier or sometimes a country. DWPE is generally based on information regarding the past violative history of the medical device and/or other information indicating that the medical device may be violative.

DWPE actions are implemented through the issuance of FDA "Import Alerts." Copies of FDA Import Alerts may be obtained at the FDA webpage under the "Field Programs" link or from the FDA Division of Import Operations and Policy. The medical glove import alert is found at: http://www.fda.gov/ora/fiars/ora_import_ia8004.html

FDA derives its authority to impose DWPE directly from section 801(a) of the Federal Food, Drug, and Cosmetic (FD&C) Act, which states that an article (device) may be refused admission:

If it **appears** from the examination of such samples or **otherwise** that:

(1) The methods used in, or the facilities and controls used for, the manufacture, packaging, storage, or installation of the device do not conform to the requirements of 520(f) (Good Manufacturing Practice Requirements)

(2) Such article is forbidden or restricted in sale in the country in which it was exported, or

(3) Such article is adulterated, misbranded, or in violation of Section 505 [New Drugs], then such article shall be refused admission.

It is important to note that the phrase **"or otherwise"** authorizes refusal of entry or detention on the basis of information **other** than the results of examination of samples. FDA may consider information such as an article's violative history as a legally sufficient reason for refusing admission under the FD&C Act. The FDA may use whatever evidence is available to evaluate the potential compliance of the medical devices offered for entry into the U.S.

Criteria for Detention Without Physical Examination (DWPE) - General

Any FDA field office, Center, or other headquarters unit may recommend devices for DWPE or for removal from DWPE when FDA believes that appropriate criteria have been met. The FDA Division of Import Operations and Policy (DIOP) routinely issues medical device specific "Import Alerts" to the FDA field offices which detail criteria for DWPE. These alerts are recommended whenever there is information suggesting that a significant number of shipments of a particular medical device or medical devices offered for import may be violative. The recommendation may be based on such information as the violative history of a medical device, manufacturer, shipper, grower, or geographic area or country. It may also be based upon other information such as knowledge of poor manufacturing or handling practices within a manufacturing facility or geographic area or country. A DWPE may be invoked **without** any previous detentions if it can be adequately supported by the submitting FDA unit.

In general, FDA recommendations can be based upon **one** violative sample collected while the medical device is in import status *or in domestic channels* if:

- The medical device may have adverse health consequences and the appropriate FDA Center concludes that the problem could warrant a Class I or II recall,

- The medical device contains actionable levels of a pesticide residue, aflatoxin or chemical contaminant,

- The medical device is violative in a way that is likely to continue due to the medical device's formulation, or

- The medical device exhibits microbiological contamination that is likely to persist.

Criteria for Release from Detention Without Physical Examination (DWPE) - General

In order for the manufacturer/shipper to be removed from the DWPE list, generally FDA must be provided with satisfactory results of sample analyses for the minimum number of consecutive shipments needed to demonstrate compliance with FDA requirements. The documentation should consist of test records (analytical worksheets) from independent qualified U.S. testing laboratories using the FDA analytical worksheet form FDA 431 or equivalent. Testing performed at the manufacturing facility or by private laboratories in the country of origin is unacceptable due to the potential for rapid degradation of gloves during shipment to the U.S. In addition, a manufacturer may provide documented evidence to demonstrate that their manufacturing operation has implemented controls as necessary for continued assurance of medical device quality. The manufacturer

may submit the appropriate documentation with a request to be removed from DWPE to the following office in FDA:

Division of Import Operations and Policy (DIOP)
5600 Fishers Lane (HFC-170)
Rockville, Maryland 20857 USA
Phone: 301-443-6553 Fax: 301-594-0413

Importers or subsidiaries may also contact the FDA near the port of entry and speak to someone who is involved with Import Operations. Callers should have their entry numbers available for reference.

In order to demonstrate compliance, manufacturers will be asked to supply a written request to the FDA which documents evidence of the current compliance status of the manufacturer's devices. Points to consider for inclusion in this written request include:

- Documentation, including FDA entry numbers showing the FDA release of the minimum number of consecutive entries of the manufacturer's devices needed to demonstrate compliance with FDA requirements, and

- A description of the manufacturer's investigation of the problem, including corrective actions, and an explanation why they believe that the problem will not reoccur.

If FDA agrees that the results of sample analysis or other evidence submitted demonstrate compliance of the manufacturer and/or medical device, the manufacturer, medical device, or country will be removed from Detention Without Physical Examination.

Import Alerts for Medical Gloves

There are currently three major import alerts under which medical gloves are commonly refused entry:

- Import Alert #80-04, "Surveillance and Detention Without Physical Examination of Surgeon's and/or Patient Examination Gloves". Manufacturers/shippers placed on this alert have had at least one previous failure of their gloves to pass an FDA analysis. This import alert consists of three increasingly more stringent levels of detention for manufacturers/shippers who repeatedly attempt to import adulterated gloves (Recidivist Firms).

- Import Alert #89-08, "Detention Without Physical Examination of Class III Medical Devices Without Approved PMA's/IDE's or Other Devices Not Found Substantially Equivalent." Manufacturers/shippers placed on this alert have not had their gloves found substantially equivalent through the 510(k) process.

- Import Alert #89-04, "Detention Without Physical Examination of Devices that have not met Device GMP's." Manufacturers/shippers placed on this alert have had a violative FDA inspection and have been issued a warning letter detailing the deviations from the QS regulation which must be corrected.

Import Alert #80-04 (Including 3 Levels of Detention for Recidivist Firms and Release Criteria)

A glove manufacturer/shipper will be placed on Import Alert #80-04 as a result of only one violative FDA analysis. The first time this occurs is referred to as Level 1 detention. If a manufacturer is placed on Level 1 detention, all shipments of gloves of the same categories (i.e., patient or surgeon's examination gloves) will be detained without physical examination, i.e., refused entry upon arrival in the U.S. In order to obtain release of the gloves placed on Level 1 or Level 2 detention the owner must provide evidence that the gloves comply with FDA requirements. For example, sample analyses performed by a qualified independent U.S. testing laboratory may be sufficient evidence to obtain admission of a detained shipment while on Level 1 or Level 2. Generally, the results of sample analyses for at least five consecutive shipments entering the U.S. which demonstrate that the gloves are in compliance with FDA requirements may be considered adequate evidence for removal from Level 1 detention.

The second time within a 24-month period that a manufacturer/shipper has a violative FDA or independent laboratory analysis, the firm will be placed on Level 2 detention. In order to be removed from IA #80-04 Level 2 detention, a manufacturer must provide increased evidence of compliance. Generally, the results of sample analyses for at least ten consecutive shipments entering the U.S. which demonstrate that the gloves are in compliance with FDA requirements may be considered adequate evidence for removal from Level 2 detention. In addition, the manufacturer is notified in writing to review their operations for QS requirements prior to shipping further products to the U.S.

The third time within the 24-month period that a manufacturer/shipper has a violative FDA or independent laboratory analysis; the FDA may issue a Warning Letter. If a Warning Letter is issued, the foreign manufacturer will be placed on Level 3 detention. At this level, analytical evidence alone may not be sufficient to show that gloves have been manufactured to meet minimum quality standards. Further evidence, such as an inspection by FDA (or in some instances, when appropriate, inspection performed by a qualified third party), to assess conformance with the QS regulation may be needed in order for a firm to be removed from Level 3 Detention. Shipments of gloves from firms on Level 3 detention may be denied entry until such evidence is provided.

Note: When a firm is on Level 2 detention, only one more violative analysis by FDA or an independent laboratory could result in placing the firm on Level 3 detention. Therefore it is recommended that firms on Level 2 detention perform a comprehensive and objective review of their manufacturing procedures and practices for conformance with the requirements of the QS regulation. If this review shows that corrections to procedures/practices are necessary to ensure gloves of acceptable quality, then such corrections should be made prior to attempting any further entries of gloves into the U.S.

Import Alert #89-04

If a manufacturer is placed on Detention Without Physical Examination for failure to comply with the requirements of the QS regulation, all shipments of medical devices from the specified

manufacturing facility will be refused entry upon arrival in the U.S. Similarly, accessories or parts for these medical devices will be detained.

To remove medical devices that were placed on Detention Without Physical Examination due to failure to comply with the QS regulation, manufacturers must:

- Correct the QS regulation deficiencies;
- Document the corrective actions that they have implemented; and
- Inform FDA of the corrections.

After FDA has reviewed the documentation explaining the corrective actions that the manufacturer has implemented or intends to implement and has determined that the corrective actions appear to be adequate, FDA will contact the manufacturer by letter. This letter will advise the manufacturer of this determination and that a reinspection will be necessary to verify the implementation of corrective actions. The CDRH Office of Compliance will request the ORO Division of Emergency and Investigations Operations to make the inspection arrangements.

Division of Emergency and Investigations Operations (HFC-130)
5600 Fishers Lane
Rockville, Maryland 20857 USA
Phone: 301-827-5653
FAX: 301-443-6919

After FDA has determined that the manufacturer is in compliance with the QS regulation, the manufacturer will receive a letter from FDA informing them that their medical devices may now be exported to the U.S., and that they have been removed from DWPE list.

Import Alert #89-08

A glove manufacturer may be placed on Import Alert #89-08 for failure to have a 510(k) premarket notification submission on file with the Agency or for failure to have a finding of substantial equivalence at the time of import. Once on Import Alert #89-08, a manufacturer will be unable to import gloves of the type(s) listed on the detention list in the alert (e.g., latex surgeon's gloves, vinyl examination gloves, powder-free latex examination gloves, etc.) This situation will continue until the Office of Device Evaluation, CDRH issues a substantial equivalence letter covering the gloves in question. The CDRH is responsible for notifying the Division of Import Operations and Policy to remove the firm from Import Alert #89-08.

FDA SAMPLING EFFORTS

It is important for foreign manufacturers who export to the U.S. and U.S. importers to understand the concept of FDA sampling, detention, and detention without physical examination. Due to limited agency resources and vast numbers of imported items, it is not possible for FDA to sample and test all imported food, drugs, cosmetics, biologics, and medical devices. Likewise, it may not be possible for an FDA sample to include all portions of, or lots present in, a shipment or container. The FDA's sampling efforts are not intended to be quality assurance testing for imported medical devices. As a consequence of limited resources, FDA field offices are constantly

attempting to apply their resources in a manner to achieve maximum efficiency. One example of improved efficiency is the use of detention without physical examination, especially for repeat violators (recidivist firms).

When a glove shipment includes multiple lots in each container it is considered a commingled shipment and FDA is not obligated to sample individual lots within the shipment. FDA may collect a sample from one or more lots out of commingled lots of gloves from a single container. Typically, FDA samples gloves from only 6 separate cartons. In this sample, FDA will attempt to represent glove sizes as they occur in the overall shipment and will attempt to include several lot numbers if present. However, exact representation in the sample is not required. Remember, all that is required to refuse entry of a shipment is the appearance of adulteration and such an appearance can be derived even from a sample that includes only one lot number or one size. If the sample fails, **all lots** are suspect and the container will be detained. In order for the importer to obtain release of commingled gloves, the importer must have the container tested **lot by lot** and identify which lots exceed defect levels. Only those lots which are shown to be in compliance, subject to verification testing by FDA, will be released for distribution in the U. S.

ENFORCEMENT STRATEGY

In addition to taking regulatory actions resulting in the refusal to permit entry of violative imported goods, the FDA has developed an enforcement strategy relative to U.S. importers who engage in business practices that appear designed to evade the lawful regulation of imports. This information is detailed in Chapter 9, Import Operations/Actions, of the FDA *Regulatory Procedures Manual* reprinted as Appendix A that follows.

Appendix A

SELECTIONS FROM THE FDA REGULATORY PROCEDURES MANUAL
Chapter 9 - Import Operations/Actions
Subchapter - Priority Enforcement Strategy For Problem Importers

PURPOSE

To provide guidance for dealing with importers or other individuals who engage in business practices that appear designed to evade the lawful regulation of imports. The procedures outlined in this chapter should not be considered all-inclusive, nor are they intended to limit local options. Situations that appear to involve criminal activity (e.g. smuggling, falsification of records) should also be referred to the Office of Criminal Investigations for their information and follow-up, as appropriate.

This guidance represents the agency's current thinking on dealing with problem importers. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public.

Priority attention should be given to firms with a history of any of the following actions:

- Distributing imported articles in domestic commerce following receipt of a Notice of FDA Action specifying the intention of Sampling, or the Detention or Refusal of the articles; or prior to receipt of a Notice of FDA Action specifying the articles are Released.

- Repeatedly importing violative articles.

- Falsifying documents at time of entry, reconditioning, or re-export, including misdeclaring articles to avoid detention without physical examination or other regulatory action.

- Re-entering previously refused articles into the United States.

- Failing to recall or redeliver to the U.S. Customs Service, at its request, an article for which a Notice of FDA Action specifying that the article was refused by FDA has been issued.

- Introducing or delivering for introduction into domestic commerce (after entry) any article which is adulterated or misbranded, or which is a new drug without an approved New Drug Application.

- Committing any prohibited act (see 21 USC 331).

BACKGROUND

In developing FDA's automated import system, known as the Operational and Administrative System for Import Support (OASIS), the specific forms "May Proceed Notice," "Release Notice," "Notice of Sampling," "Notice of Detention and Hearing," and "Notice of Refusal" have been replaced by the issuing of "Notices of FDA Action," which includes a description of the specific

FDA action (May Proceed, Release, Sampling or Intention of Sampling, Detention, or Refusal) identified for the specific line in the entry. The use of the designations "Product May Proceed," "Product Released by FDA," "Product Collected by FDA," "Product Detained by FDA," or "Product Refused Entry by FDA," or similar wording should be considered as meeting the standard, "giving notice thereof to the owner or consignee." (See 21 USC 381(a); 21 CFR 1.94.)

In 1988, the Agency conducted a short-term enforcement operation aimed at determining the disposition of food articles refused admission. Thirteen percent of articles refused admission for non-labeling violations had been distributed in interstate commerce, rather that redelivered for export or destruction.

In 1990, the Agency discovered an importer of ceramic dinnerware circumventing detention without physical examination by declaring the entries as statuary, a non-regulated article.

Between 1990 and 1992, New York District, in conjunction with the U.S. Customs Service, investigated and documented an importer's history of violative practices regarding the importation of frozen seafood products. Practices included repeatedly importing violative articles; falsifying documents and manipulating articles to avoid detention without physical examination; refusing or not permitting timely inspection of entries; importing previously refused articles; and smuggling. As a result of the investigation, in 1992 the firm's president was indicted by the U.S. District Court in New Jersey. He was subsequently convicted on 138 counts for submitting false documents to FDA and for illegally re-importing previously rejected salmonella contaminated seafood. On February 5, 1993, all frozen seafood products imported by the firm were placed on detention without physical examination.

Between 1992 and 1995, Florida District and the Office of Criminal Investigations, in conjunction with the U.S. Customs Service, investigated and documented an importer's history of violative practices regarding the importation and handling of frozen shrimp. Practices included repeatedly importing violative articles; falsifying documents to avoid detention without physical examination; manipulating articles in attempts to have packers removed from detention without physical examination; and laboratory shopping (sending samples of product that is detained without physical examination to different private labs and then submitting to FDA only the analysis which shows the product in compliance, even though the other lab found the product violative). Further, Florida District identified three shipments of shrimp imported by the firm which were seized because of decomposition. Prior to the seizures, the firm attempted to sell the decomposed shrimp, which had been rejected by eight consignees and the National Marine Fisheries Service. The firm also was discovered washing decomposed, imported shrimp with a copper sulfate solution in an attempt to conceal the decomposition. On March 10, 1995, all frozen shrimp imported by the firm was placed on detention without physical examination. As a further result of the investigation, the firm and its top management were indicted by the U.S. District Court in Florida. The firm's vice president was convicted on 12 felony counts, including conspiracy, obstructing justice, violating Customs law, and tainting shrimp and selling it with the intent to defraud and mislead.

APPROACH

The following enforcement approaches have general applicability. They should be considered when dealing with firms engaged in the types of practices listed in the "Purpose" section above, when conventional import coverage and enforcement avenues appear insufficient to address the

problem. The approaches include review and approval of reconditioning proposals (FD-766), the use of Warning Letters (sequential, when appropriate), recall, seizure, injunction, or prosecution.

As always, use of enforcement discretion by the district should be considered in determining the appropriate regulatory response. When egregious actions are encountered, a sequential approach may not be appropriate. Also, situations that appear to involve criminal activity (e.g., smuggling, falsification of records) should be referred to the Office of Criminal Investigations for their information and follow-up, as appropriate.

WARNING LETTERS

Issuance of Warning Letters to remind firms of their responsibilities to import articles that comply with the provisions of the Federal Food, Drug, and Cosmetic Act and other laws enforced by FDA, and to assure that only non-violative articles enter domestic commerce in the United States, is often an appropriate first action. (Refer to RPM Subchapter, "Warning Letters.") Warning Letters may be issued to the importer of record, owner, or consignee (if other than the importer of record) with copies to Customs, and may be issued for the following reasons:

1. Failure to hold an entry intact pending receipt of a Notice of FDA Action specifying that the article was Released by FDA. A copy of the Warning Letter should be attached to the redelivery request sent to Customs when such a request is made.

2. The first documented attempted entry with misleading information. Misleading information includes, for example, low-acid canned foods from a non-registered plant entered under another processor's Food Canning Establishment (FCE) number; or articles from firms subject to detention without physical examination; or articles declared as non-regulated articles to avoid detention without physical examination or other agency action.

3. The first documented instance of submission of a foreign government certification document or private laboratory analytical report that does not match the entry in question.

4. An importer's failure to provide FDA with information regarding the availability for sampling or location of an entry for which a Notice of FDA Action specifying FDA's intention of sampling has been issued.

5. To inform an importer that FDA has requested that Customs deny it permission to file an entry bond, thus restricting its shipments to Customs' custody until admissibility has been determined.

6. Consistently importing violative articles not already subject to detention without physical examination. The importer should be notified that this practice may result in future entries being detained without physical examination.

7. Any other situation which warrants an official notification to the firm and further opportunity for compliance before other action is taken.

The Warning Letter should state that any distribution of refused articles or articles sampled or intended for sampling that were distributed prior to release are in violation of the Federal Food,

Drug, and Cosmetic Act or other applicable acts enforced by FDA, and may result in domestic seizure or other sanctions, including injunction or prosecution.

RECONDITIONING PROPOSALS

The Federal Food, Drug, and Cosmetic Act provides that when an article submitted for entry is found to be violative, the importer has the option of exporting it, destroying it, rendering it not subject to the Act, or requesting permission from the agency to attempt to bring it into compliance with the Act.

If the importer of record decides to attempt to recondition a detained article, section 801(b) of the Act (21 USC 381 (a)) provides that the owner or consignee (by practice, FDA also accepts applications from an importer of record, with a properly posted bond, as the agent of the owner or consignee) may submit to the FDA a written application (Form FD-766 or other acceptable means) requesting permission to bring into compliance an article that is adulterated, misbranded, or in violation of Section 505 (see 21 USC 381 (a)(3)). The owner or consignee may bring the article into compliance by relabeling or other action, or by rendering it other than a food, drug, device, or cosmetic. (Refer to RPM Subchapter, "Reconditioning.")

The approval of the reconditioning application is at FDA's discretion. The Agency should require appropriate controls and provisions as a part of any application before it approves the reconditioning. The application is an agreement between the importer (or other appropriate party submitting the application) and the Agency.

If FDA has documented an importer's practice of consistently importing violative articles not already subject to detention without physical examination and only attempting to recondition the articles after detention, the District may require, as part of any reconditioning application, that the importer agree to destroy any article not brought into compliance during reconditioning, in lieu of permitting re-export of the violative article.

Districts should consult and obtain the concurrence of both the ORO/Division of Import Operations and Policy (DIOP) and the appropriate Center Compliance Office before initiating a policy requiring a specific importer to destroy rather than re-export violative articles as part of every reconditioning process. The information supplied should include, but not be limited to, the following:

1. Documentation of the firm's pattern of importing violative articles.

2. Documentation of prior warning to the firm of their obligation to import the article in compliance with the Federal Food, Drug, and Cosmetic Act or other acts enforced by FDA.

3. Documentation which may establish that the article can be imported in compliance and thus would not require reconditioning after importation.

REQUESTS FOR VOLUNTARY RECALLS

Although requests for voluntary recalls duplicate a request for redelivery action to some degree, they also offer definite advantages. Experience indicates that requesting the firm to initiate a voluntary action, such as a recall, may result in a more favorable response by the firm than a demand for redelivery. A recall may occur more promptly because it can be initiated in a matter of days, while redelivery may not take place for 90 days or more. This is especially significant in hazard-to-health situations. A recall may provide FDA with further knowledge of the status of the violative merchandise being returned and usually makes it easier to maintain control of the article. This ultimately leads to improved consumer protection.

District management should very carefully encourage the firm to consider a voluntary recall under the following situations:

1. When a potential health hazard situation exists.

2. When there is evidence of distribution of detained or refused merchandise.

When an importer fails to respond fully or in a timely manner to a Warning Letter, or we are notified by Customs that an Importer has not responded to a Notice of FDA Action Specifying Refusal of the product, it may be an indication the goods are no longer intact. A visit to the importer may be appropriate and, if articles are missing, attempt to determine the firm's intentions with respect to corrective action.

When a potential health hazard situation exists and the article has been illegally distributed, appropriate press coverage may issue naming firm, product, and country of origin. Issuance of all publicity must be in accordance with guidelines.

Import recalls are to be conducted in full accordance with the guidelines in RPM Subchapter, "Recall Procedures." Supervision of the disposition of returned articles may be made either by FDA or Customs. If disposition will be by destruction, it is suggested that FDA provide the supervision. If the articles are to be exported, Customs or FDA may handle the supervision.

SEIZURE

Seizure is another enforcement approach that may be considered to gain control over violative imported articles. Seizure is an action against an article. Consequently, it will be necessary to show, through laboratory analysis or otherwise, that the article seized is actually violative. An importer's history of illegal actions, while relevant, is not itself sufficient to support seizure. Whatever the importer's previous history, it will be necessary to show that the article itself is violative.

Seizure may be considered for an article which:

1. Represents a potential hazard to health and has been or is likely to be distributed in domestic commerce following receipt of a Notice of FDA Action specifying that the article is Detained or Refused; or

2. Has been fraudulently identified/represented in documents submitted to the Agency; or

3. Is identified by the Agency as a previously refused article.

When an imported article is seized, and condemned, it is subject to the provisions of section 304(d) (21 USC 334(d)) which may allow for re-exportation of the article, provided specified conditions are met. Under 21 USC 334(d), certain condemned imported articles may be re-exported under limited circumstances. Re-exportation is not available for condemned unapproved new drugs (see 21 USC 355), or foods in violation of the emergency permit control provision (see 21 USC 344). Such articles must be destroyed.

In order to be able to re-export condemned imported articles, the party seeking re-export must satisfy several threshold conditions:

1. The violation did not occur after the article was imported.

2. The party seeking re-export "had no cause for believing that it was adulterated, mis-branded, or in violation before it was released from Customs custody."

3. The party seeking re-export must "establish that the article was intended for export at the timethe article entered commerce." An example of where it may be possible to demonstrate that a product was intended for export at the time it entered commerce would be when products are imported for purpose of transshipment to a destination outside the U.S.

4. Compliance with 21 USC 381 (e) (1):

    a. Intended for export.

    b. Accords with the specifications of the foreign purchaser (unless the article is to be exported to the original foreign supplier, in which case there is no need to comply with this requirement).

    c. May not be in conflict with the laws of the country to which it is intended for export unless the article is to be exported to the original foreign supplier, in which case there is no need to comply with this requirement).

    d. Labeled on the outside of the shipping package that it is intended for export.

    e. Not sold or offered for sale in domestic commerce.

Therefore, there are circumstances where the seizure of an article may not accomplish more than detention and refusal of the article, other than stricter control over the goods before re-export and compliance with the applicable requirements of Section 801(e) (21 USC 381(e).

Consequently, in evaluating whether a seizure is an appropriate course of action, a district should consider whether the facts in the case would justify recommending to a court that re-export of the article would be an unsatisfactory resolution. Among the points to consider are:

1. Does a potential health hazard exist?

2. Does the previous history of the person in possession of the articles indicate that the person may attempt to re-enter the articles into the United States at a later date?

3. Did the violation occur after the article was imported?

4. Did the importer have cause to believe that the article was in violation before entry?

5. Does the article meet the legal specifications of the country to which it would be exported?

6. Was any portion of the article sold or offered for sale in domestic commerce?

7. Is the article in violation of 21 USC 342(a)(1), (2), or (6), 344, 351(a)(3), 352(j), 355 or 361(a) or (d)?

8. If the article is a drug will it be re-exported to the original foreign supplier?

Under certain circumstances, the district may recommend seizure of violative articles under 21 USC 334 while the articles are still under import status, rather than allow re-export as provided under 21 USC 381 (a). Generally, seizure of articles while in import status may be appropriate if the articles must be destroyed (pose a serious health hazard or it is likely that the articles will be reintroduced into the United States), or the public health requires that certain conditions be imposed (e.g., conditions in 21 USC 381(e)(1)).

As with citation, prosecution, and injunction, samples collected for seizure consideration should, whenever possible, include a 702(b) portion (see 21 USC 372 (b)). Such samples should be collected, sealed, analyzed, and otherwise handled in accordance with procedures normally applied to domestic samples.

State embargo authority and Customs holds are alternative methods to gain control over violative articles. Customs may also release an article at our request so that an immediate domestic seizure may be conducted. Moreover, if a violative article represents evidence of a crime, it may be seized pursuant to a criminal search and seizure warrant. These avenues should also be considered, especially if an importer is likely to attempt to quickly re-export the article.

INJUNCTION

If injunction is the action of choice, the case should be developed in accordance with the procedures set forth in RPM Subchapter, "Injunctions." Injunctions may require a pattern of actual violations with some recognizable danger of a recurrence. The monitoring of an injunction is resource intensive. These facts should be taken into consideration when evaluating this course of action. Also consider that an injunction often results in a hearing more quickly than does a prosecution, particularly if a Temporary Restraining Order (TRO) is requested. This can result in quick corrective action as well as more rapid and efficient redelivery if this response is requested in the injunction. Also, the burden of proof is less in civil cases than in criminal cases, and injunction does not preclude subsequent prosecution for the same violation.

When developing an injunction case against an importer or consignee, there must be a well-documented history of an illegal practice.

A TRO requires a heightened showing of harm. See RPM Subchapter, "Injunctions" regarding the prerequisites for a TRO in conjunction with an injunction action.

CITATION/PROSECUTION

Citation/prosecution should be used when conventional import enforcement approaches are determined to be inadequate to correct violative practices, or the violation is sufficiently egregious to warrant punishment.

When citation/prosecution is the action of choice, refer to RPM Subchapters, "Citations" and "Prosecution" for the appropriate procedures.

Districts should consider the potential impact of developing citation/prosecution recommendations as the action of choice in the following instances:

1. Where there is repetitive illegal distribution of articles after issuance of a Notice of FDA Action specifying the intention of Sampling or Detention; or

2. Where the importer submits false or misleading entry documents; or

3. Where the importer submits false or misleading private laboratory analytical results or false certifications; or

4. Where the importer submits false or misleading export documents; or

5. Where the importer repeatedly brings previously refused articles into the United States; or

6. Where evidence of other fraud exists.

This list is not all inclusive and there may be other situations where citation/prosecution is appropriate.

Any recommendation for citation, prosecution, or injunction must be supported by fully documented instances of attempts to circumvent normal import procedures. For a felony prosecution recommendation, there must be a fully documented attempt to do the same, with evidence of the intent to defraud or mislead. It is not necessary, in developing a citation/prosecution recommendation, to show that each specific entry is actually violative. However, physical evidence that documents the violative nature of an entry (or of several entries) would be useful to highlight the likely result of the firm's pattern of behavior.

It is important to remember that sample collection and analytical procedures in these cases, as for seizures and injunctions, should differ from routine import work. The Office of Chief Counsel has consistently advised us that when an import physical sample is collected for use in an anticipated legal action, a sealed 702(b) portion should be available (21 USC 372 (b). This request is further supported by guidance provided in the RPM. Proper chain of custody should also be maintained

for these samples. Ordinarily, check analyses should be conducted on such samples. In instances where Compliance Policy Guides exist and instructions differ for domestic legal actions as opposed to import detention, districts should follow the guidance for domestic legal actions in terms of types of analyses, check analyses, etc.

Importers of articles detained without physical examination should not feel free to distribute and sell such articles without risk of criminal penalty. Criminal action may be possible against importers violating FDA's detention without physical examination actions or who routinely ship articles without a Notice of FDA Action indicating the articles are Released. Refusal to allow inspection is a violation of the Federal Food, Drug, and Cosmetic Act. Subsequent entry pursuant to an inspection warrant may yield evidence providing the basis for a felony violation for refusal to allow inspection. Distribution of an article prior to receipt of a Notice of FDA Action indicating the article May Proceed or is Released should be considered refusal to permit inspection, as authorized by section 704 (21 USC 374).

In addition to charges under the Federal Food, Drug, and Cosmetic Act and Customs law, Title 19 (note especially, 19 USC 1592 and 1595a), and/or Title 18 charges may also be considered. These include 18 USC 1001, false statements; 18 USC 1505, obstruction of justice (when a firm knowingly and willingly interferes with an FDA inspection by distributing imported articles not released by FDA from import status); 18 USC 542, entry by use of a false statement; 18 USC 545, smuggling; and 18 USC 371, conspiracy.

The following is an excerpt from FDA Compliance Policy Guides, Chapter 3 - Devices.

Appendix B

SEC. 335.700 SURGEONS' GLOVES AND PATIENT EXAMINATION GLOVES; DEFECTS - CRITERIA FOR DIRECT REFERENCE SEIZURE (CPG 7124.31)

BACKGROUND:

Surgeon's and patient examination gloves have been increasingly relied upon by health care workers as a barrier to the transmission of Human Immunodeficiency Virus (HIV) and other blood and fluid-borne infectious agents. On August 21, 1987, the Centers for Disease Control recommended that health care workers wear medical gloves routinely because of the potential for transmission of HIV between patients and health care workers. Because hard to detect glove defects, such as holes, can compromise the effectiveness of the glove barrier and pose risk to the health of both patients and health care workers, FDA issued guidelines to the field districts on September 28, 1988, to sample and analyze surgeon's and patient examination gloves of both domestic and foreign origin. Gloves were leak tested using the 1000 ml water method. Regulatory actions under existing authority, such as seizures and detentions of specific glove lots, were handled on a case by case basis. Surgeon's glove lots with failure rates of 10% (10 units in 100) or higher, and patient examination gloves with failure rates of 20% (20 units in 100) or higher were subject to regulatory action. In view of the rapid increase in demand for imported and domestically produced gloves, and the public health benefits of further reducing the risk of transmission of HIV and other blood and fluid borne infectious agents, and to better utilize Agency resources, on November 21, 1989, FDA published in the Federal Register proposed rules to insure that manufacturers of gloves manufacture gloves that are not adulterated. The final rule was published on December 12, 1990, at 55 FR 51254.

FDA will collect samples from lots of gloves to perform the test for defects by the water leak method using 1000 mL water as described in paragraph (b) Test Method of the final rule entitled "Patient examination gloves and surgeon's gloves; sample plans and test method for leakage defects; adulteration." 55 FR 51256 - 51258; 21 CFR 800.20.

The sampling inspection plan used by the FDA has been derived from MIL-STD-105E (the military standard for "Sampling Procedures and Tables for Inspection by Attributes"), based on general inspection level II, normal inspection, and an acceptable quality level (AQL) of 2.5% for surgeon's gloves and 4.0% for patient examination gloves. Single sampling will be used for lots less than or equal to 1200 gloves, while multiple sampling will be used for larger lots. [The FDA sampling inspection plan is described below in 21 CFR 800.20 (c).]

POLICY:

Surgeon's gloves and patient examination gloves that contain holes are adulterated devices. Adulteration will be determined on a lot by lot basis for enforcement purposes. [See 21 CFR 800.20.] Surgeon's gloves whose leakage defect rate exceeds an AQL of 2.5% and patient examination gloves whose leakage defect rate exceeds an AQL of 4.0% will be deemed actionable as described in 21 CFR 800.

REGULATORY ACTION GUIDANCE:

Lots of surgeon's and patient examination gloves that fail the criteria in Attachment A "Sampling Inspection Plan" are subject to direct reference seizure. Districts should forward seizure recommendations to the Division of Compliance Management and Operations (HFC-210).

SPECIMEN CHARGES:

NOTE: Complaints for the seizure of devices should not include allegations of shipment in interstate commerce because allegations of interstate commerce are not required to support seizure of devices [see section 304(a)(2)] .

For lots of surgeon's gloves which are found to be defective at an AQL greater than 2.5%, and for lots of patient examination gloves which are found to be defective at an AQL greater than 4.0% charge:

> "The article is deemed adulterated within the meaning of the Act, 21 U.S.C. 351(c) because the quality of the gloves falls below that which it purports or is represented to possess in that the defect rate of the gloves exceeds the permissible rate identified at 21 CFR 800.20."

The proposed letter to the U.S. Attorney should also include the following two paragraphs (fill in the blanks with the appropriate numbers):

> Examination gloves are intended for use by health professionals such as physicians and dentists during routine medical and dental examinations. Health professionals rely on examination gloves to prevent the transmission and spread of disease. This has become increasingly important in light of the current AIDS epidemic.
>
> We request seizure because analysis of the gloves by the Food and Drug Administration (FDA) shows that their quality falls below that which it purports and is represented to possess because the defect rate of the gloves exceeds the permissible level as set forth in 21 CFR. ___ out of ___ gloves tested were found to leak or contain holes. 21 U.S.C. 351(c).

The following is taken from 21 CFR Part 800 and contains sample plans and test methods for leakage defects and adulteration of patient examination gloves and surgeon's gloves.

Appendix C
21 CFR, TITLE 21, VOLUME 8

[1]

[Code of Federal Regulations]
[Title 21, Volume 8, Food and Drugs, Parts 800 to 1299]
[Revised as of April 1, 1996]
From the U.S. Government Printing Office via GPO Access
[CITE: 21 CFR 800.20]

TITLE 21--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES--(Continued)

PART 800 --GENERAL

Subpart B--Requirements for Specific Medical Devices

Sec. 800.20 Patient examination gloves and surgeons' gloves; sample plans and \ test method for leakage defects; adulteration.

(a) Purpose. The prevalence of human immunodeficiency virus (HIV), which causes acquired immune deficiency syndrome (AIDS), and its risk of transmission in the health care context, have caused the Food and Drug Administration (FDA) to look more closely at the quality control of barrier devices, such as surgeons' gloves and patient examination gloves (collectively known as medical gloves) to reduce the risk of transmission of HIV and other blood-borne infectious diseases. The Centers for Disease Control (CDC) recommend that health care workers wear medical gloves to reduce the risk of transmission of HIV and other blood-borne infectious diseases. The CDC recommends that health care workers wear medical gloves when touching blood or other body fluids, mucous membranes, or nonintact skin of all patients; when handling items or surfaces soiled with blood or other body fluids; and when performing venipuncture and other vascular access procedures. Among other things, CDC's recommendation that health care providers wear medical gloves demonstrates the proposition that devices labeled as medical gloves purport to be and are represented to be effective barriers against the transmission of blood- and fluid-borne pathogens. Therefore, FDA, through this regulation, is defining adulteration for patient examination and surgeons' gloves as a means of assuring safe and effective devices.

(1) For a description of a patient examination glove, see Sec. 880.6250. Finger cots, however, are excluded from the test method and sample plans in paragraphs (b) and (c) of this section.

(2) For a description of a surgeons' glove, see Sec. 878.4460 of this chapter.

(b) Test method. For the purposes of this regulation, FDA's analysis of gloves for leaks will be conducted by a water leak method, using 1,000 milliliters (mL) of water. Each medical glove will be analyzed independently. When packaged as pairs, each glove is considered separately, and both

[1] Sketches of the test apparatus described in this Federal Register are shown in Fig 1 and Fig 2 at the end of the FR text.

gloves will be analyzed. A defect on one of the gloves is counted as one defect; a defect in both gloves is counted as two defects. Defects are defined as leaks, tears, mold, embedded foreign objects, etc. A leak is defined as the appearance of water on the outside of the glove. This emergence of water from the glove constitutes a watertight barrier failure. Leaks within 1 and \1/2\ inches of the cuff are to be disregarded.

(1) The following materials are required for testing: A 2\3/8\-inch by 15-inch (clear) plastic cylinder with a hook on one end and a mark scored 1\1/2\ inches from the other end (a cylinder of another size may be used if it accommodates both cuff diameter and any water above the glove capacity); elastic strapping with Velcro or other fastening material; automatic water-dispensing apparatus or manual device capable of delivering 1,000 mL of water; a stand with horizontal rod for hanging the hook end of the plastic tube. The support rod must be capable of holding the weight of the total number of gloves that will be suspended at any one time, e.g., five gloves suspended will weigh about 11 pounds.

(2) The following methodology is used: Examine the sample and identify code/ lot number, size, and brand as appropriate. Examine gloves for defects as follows: carefully remove the glove from the wrapper, box, etc., visually examining each glove for defects. Visual defects in the top 1\1/2\ inches of a glove will not be counted as a defect for the purposes of this rule. Visually defective gloves do not require further testing but are to be included in the total number of defective gloves counted for the sample. Attach the glove to the plastic fill tube by bringing the cuff end to the 1\1/2\-inch mark and fastening with elastic strapping to make a watertight seal. Add 1,000 mL of room temperature water (i.e., 20 deg. C to 30 deg. C) into the open end of the fill tube. The water shall pass freely into the glove. (With some larger sizes of long-cuffed surgeons' gloves, the water level may reach only the base of the thumb. With some smaller gloves, the water level may extend several inches up the fill tube.)

(3) Immediately after adding the water, examine the glove for water leaks. Do not squeeze the glove; use only minimal manipulation to spread the fingers to check for leaks. Water drops may be blotted to confirm leaking. If the glove does not leak immediately, keep the glove/filling tube assembly upright and hang the assembly vertically from the horizontal rod, using the wire hook on the open end of the fill tube (do not support the filled glove while transferring). Make a second observation for leaks 2 minutes after addition of the water to the glove. Use only minimal manipulation of the fingers to check for leaks. Record the number of defective gloves.

(c) Sample plans. FDA will collect samples from lots of gloves to perform the test for defects described in paragraph (b) of this section in accordance with FDA's sampling inspection plans which are based on the tables of MIL-STD-105E (the military sampling standard, ``Sampling Procedures and Tables for Inspection by Attributes," May 10, 1989). Based on the acceptable quality levels found in this standard, FDA has defined adulteration as follows: 2.5 or higher for surgeons' gloves and 4.0 or higher for patient examination gloves at a general inspection level II. FDA will use single normal sampling for lots of 1,200 gloves or less and multiple normal sampling for all larger lots. For convenience, the sample plans (sample size and accept/reject numbers) are shown in the following tables:

Adulteration Level at 2.5 for Surgeons' Gloves

Lot size	Sample	Sample size	Number examined	Number defective	
				Accept	Reject
35,001 and above	First	125	125	2	9
	Second	125	250	7	14
	Third	125	375	13	19
	Fourth	125	500	19	25
	Fifth	125	625	25	29
	Sixth	125	750	31	33
	Seventh	125	875	37	38
35,000 to 10,001	First	80	80	1	7
	Second	80	160	4	10
	Third	80	240	8	13
	Fourth	80	320	12	17
	Fifth	80	400	17	20
	Sixth	80	480	21	23
	Seventh	80	560	25	26
10,000 to 3,201	First	50	50	0	5
	Second	50	100	3	8
	Third	50	150	6	10
	Fourth	50	200	8	13
	Fifth	50	250	11	15
	Sixth	50	300	14	17
	Seventh	50	350	18	19
3,200 to 1,201	First	32	32	0	4
	Second	32	64	1	6
	Third	32	96	3	8
	Fourth	32	128	5	10
	Fifth	32	160	7	11
	Sixth	32	192	10	12
	Seventh	32	224	13	14
1,200 to 501	Single sample		80	5	6
500 to 281	Single sample		50	3	4
280 to 151	Single sample		32	2	3
150 to 51	Single sample		20	1	2
50 to 0	Single sample		5	0	1

Adulteration Level at 4.0 for Patient Examination Gloves

Lot size	Sample	Sample size	Number examined	Number defective	
				Accept	Reject
10,001 and above	First	80	80	2	9
	Second	80	160	7	14
	Third	80	240	13	19
	Fourth	80	320	19	25
	Fifth	80	400	25	29
	Sixth	80	480	31	33
	Seventh	80	560	37	38
10,000 to 3,201	First	50	50	1	7
	Second	50	100	4	10
	Third	50	150	8	13
	Fourth	50	200	12	17
	Fifth	50	250	17	20
	Sixth	50	300	21	23
	Seventh	50	350	25	26
3,200 to 1,201	First	32	32	0	5
	Second	32	64	3	8
	Third	32	96	6	10
	Fourth	32	128	8	13
	Fifth	32	160	11	15
	Sixth	32	192	14	17
	Seventh	32	224	18	19
1,200 to 501	Single sample		80	7	8
500 to 281	Single sample		50	5	6
280 to 151	Single sample		32	3	4
150 to 91	Single sample		20	2	3
90 to 26	Single sample		13	1	2
25 to 0	Single sample		3	0	1

(d) Lots of gloves which are tested and rejected using the test method according to paragraph (b) of this section, are adulterated within the meaning of section 501(c) of the Federal Food, Drug, and Cosmetic Act, and are subject to regulatory action, such as detention of imported products and seizure of domestic products. [55 FR 51256, Dec. 12, 1990]

Fig 1

Фіг 5